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# THE GENETICS OF MUCOPOLYSACCHARIDOSES

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This review aims to summarize scientific data on the contribution to the study of hereditary lysosomal disease - mucopolysaccharidoses. The article presents a review of the literature on the clinical picture and diagnosis of mucopolysaccharidosis in patients, the frequency of these diseases in the world is given. The available medical literature on the study of MPS was analyzed using the PubMed database, eLIBRARY.RU, Google Academia

**Keywords:** mucopolysaccharidosis.

**Introduction.** The first information about disorders of lysosomal accumulation appeared at the end of the 19th century, and Tay-Sachs disease was first described in 1881 and 1882. The disease was named after doctors Warren Thau and Bernard Sachs and French dermatologist Philippe Gauche. 50 years later, in 1932, Dutch physician John Pompei announced the type II glycogen disease that would later become his name. Pompe disease is the first hereditary disease to be identified as a lysosomal storage disorder. Lysosomes were discovered experimentally between 1949 and 1952, when the biochemist Christian de Dube and colleagues discovered that they were the organelles responsible for the intracellular degradation and reuse of macromolecules. This finding further elucidates the pathophysiological basis of lysosomal storage disorders. After the first clinical phenotype was identified in the 19th century, lysosomes were recognized in 1955/56, and since 1963 the biochemical defects underlying LSD have been proven and knowledge of LSD has increased. In the 1970s and 1990s, research focused on the mannose phosphate 6 receptor pathway, the sorting mechanism of lysosomal enzymes, the identification of the molecular basis of LSD, and the development of tools and strategies to investigate lysosomal biology. Attempts to treat these diseases with enzyme replacement therapy were first made in the 1990s. Currently, research is focused on the role of lysosomes as signaling platforms for the control of cellular

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metabolism and the development of new therapies.

Glucosaminoglycans are polysaccharides composed of hexosamine amino sugars, which are the carbohydrate portion of proteoglycans. In the body, glycosaminoglycans are covalently linked to the protein portion of the proteoglycan and do not exist in free form. In the past, mucopolysaccharides were called mucopolysaccharides because they were contained in the secretions of the mucosa (mucosa), giving them viscosity and lubricity. Together with GAG, proteoglycans are important components of the extracellular matrix and play an important role in intercellular interactions, the formation and maintenance of the shape of cells and organs, and the formation of the skeleton for tissue formation, in particular by interacting with collagen, elastin, fibronectin, laminin and other extracellular matrix proteins. . Since it is a polyanion, in addition to water, a large number of cations (Na +, K +, Ca2 +) can be attached, which are involved in the formation of tension in various tissues and can prevent the spread of pathogenic microorganisms. [2,18,22,27]

Currently, there are 6 types of glycosaminoglycans: chondroitin-4-sulfate (chondroitin sulfate A), chondroitin-6-sulfate (chondroitin sulfate C), dermatan sulfate, keratan sulfate, heparan sulfate and hyaluronic acid.

Excessive accumulation of glycosaminoglycans in organs and tissues causes damage and swelling of organs containing a large amount of extracellular matrix. In this case, lysosomes accumulate incompletely destroyed glycosaminoglycans and fragments of their oligosaccharides, which are excreted in the urine.

**Mucopolysaccharidosis type I.** Mucopolysaccharide disease (MPS) type I (ICD10: E 76.0) is a disease caused by a mutation in the IDUA gene that causes a deficiency or a significant decrease in the activity of the enzyme α-L-idronidase. Inhibition by enzyme mutations is a chronic progressive disease with disorders of various organs and systems, including the skeletal system, cardiovascular system, central nervous system, and ophthalmic system [28]. The incidence was wide: 1:10 million ~ 1:14 million in Harra syndrome, 1:30 million and 1:64 million in Chai and Morcio syndrome [26].

In 1919, the German pediatrician Gertrud Harler reported patients with characteristic skeletal disorders, mental retardation, and corneal clouding. This type of disease was later called "Pfaundler-Hurler syndrome". In connection with the appearance of the phenotype of the patient, similar to the gargoyle, in 1936 the British doctor R. Ellis suggested another name for the disease - "Gargoyle disease". In 1962, Dr. Scheie, an ophthalmologist, described a patient with corneal clouding with mild disease. This disease is called Scheye's syndrome, and for some time was considered a type of mucopolysaccharidosis. However, in 1971 it was discovered that Scheye's syndrome and Hurler's syndrome were the same cause of decreased activity of an enzyme called α-L-idronidase. Subsequently, several cases of an intermediate type have been reported. They were not classified as severe or mild and were classified as more severe Scheye syndrome. It has been found that MPS type I is caused by mutations in the same gene, but its clinical manifestations are very diverse [28].

Currently, 3 types of phenotypes have been reported: Hurler syndrome (MPS type IH - severe type), Scheye syndrome (MPS type - mild type) and Hurler-Scheye syndrome (MPS type I H/S - intermediate type). More than 90 mutations have been identified in the α-L-IDUA gene. In α-L-idronidase deficiency, dermatan sulfate and heparan sulfate accumulate in lysosomes, causing damage to various organs and systems [14, 15, 16]. With Hurler's syndrome, the first signs appear already in the 1st year of life. The main clinical symptoms are short stature, short neck, scaphocephaly, microcephaly, coarse facial features, full lips, wide nostrils, sunken nose bridge, eye hypertelorism, small sparse teeth (Hurler phenotype), hepatosplenomegaly, deafness, umbilical and inguinal hernia. Later, as the patient develops, deep dementia, stiffness in large and small joints, scoliosis, kyphosis, hearing and vision impairment, obstructive sleep apnea syndrome, heart failure, etc. develop. Due to the rapid progression of the disease, he may also die within 10 years of birth [26,28].

Scheye syndrome - with this form of joint stiffness manifesting at the end of the first decade of life and characterized by slow progression, growth and intelligence do not suffer. Facial features very gradually coarsen and change according to the type of gargoilism ("broad-short face"). Multiple dysostosis is mainly represented by stiffness of the joints of the hands, the formation of a "clawed paw", painful stiffness of the feet, hollow foot, valgus deformity of the knee joints. Carpal tunnel syndrome often develops, which, along with stiffness, leads to limited function of the upper extremities [26].

The intermediate form of MPS, IH/S (Hurler-Scheie syndrome), is characterized by normal and subnormal intelligence with progressive somatic pathology and multiple dysostosis. The disease manifests itself in childhood, at the age of 3-8 years. The course of the disease is progressive. Joint stiffness, sensorineural hearing loss, corneal clouding, airway obstruction, cardiovascular pathology in the form of valve damage, myocardial thickening, systemic and pulmonary hypertension, narrowing of the coronary arteries up to a heart attack. Micrognotia of facial shape and hydrocephalus.

**Mucopolysaccharidosis type II.** Mucopolysaccharide type II (Hunter's syndrome) (ICD10: E 76.1) is a serious progressive disease caused by a deficiency of the enzyme iduronate-2-sulfatase. The genetic form is X-linked recessive, so it mostly develops in males. However, there are isolated cases of Hunter syndrome in women due to mutations in the IDS gene on the maternal X chromosome and asymmetric inactivation of the paternal X chromosome [24].

The incidence of MPS type II in newborn boys ranges from 1:100,000 to 1:132,000 [25]. In 1980, Schaap and Bach studied the incidence of Hunter syndrome in boys in Israel, which was 34,000 per 1 newborn [16].

The IDS gene was mapped to the long arm of the X chromosome Xq28. Although the range of mutations found in Hunter syndrome is very wide. The phenotype is extremely heterogeneous and rather conditionally subdivided into severe and mild forms, representing in fact a continuum of clinical phenotypes differing in severity [16,24]

In severe form, it differs little from Hurler's syndrome, although it is characterized by a slower progression of somatic and neuropsychiatric symptoms and some features of the clinical phenotype (absence of corneal opacity, less severe mental retardation). The course of the disease is progressive. Manifestation of the disease at 3 years of age. Severe neurological symptoms (encephalopathy, decreased motor activity to immobility, cachexia, lack of response to the environment, severe mental retardation). At an early age, they suffer from frequent respiratory diseases. Corneal opacity is uncommon in MPS II, but patients may have severe retinal degeneration. The pathognomonic symptom of the disease is combined heart defects (mitral valve stenosis, severe diffuse insufficiency of the coronary circulation). Patients die at the age of 10–15 years from airway obstruction or heart failure. [6,24].

The mild form bears clinical resemblance to Scheye's syndrome and is characterized by normal or subnormal

intelligence with slowly progressive somatic pathology and slowly developing multiple dysostosis. [37]. The manifestation of the disease is 3–8 years, for benign forms at 10–15 years. As a rule, the patient's intelligence is not impaired. In some cases, there is also the possibility of mild mental retardation. Patients often live to age 30 or older [2,6,16,24].

**Mucopolysaccharidosis type III.** The Sanfilippo syndrome, a clinical manifestation of type III MPS, was first reported in 1963 by the American pediatrician Sylvestra Sanfilippo, a patient with behavioral disorders and reduced psycholinguistic development.

The incidence of MPS type III ranges from 1:58,000 to 1:100,000 in MPS IIIA and MPS IIIB [7].

Due to the deficiency of enzymes involved in the degradation of heparan sulfate, 4 subtypes are currently known. MPS IIIA, alpha-N-acetylglucosaminidase in MPS IIIB, acetyl-CoA-α-glucosaminide-N-acetyltransferase in MPS IIIC, and N-acetylglucosamine 6-sulfatase in MPS IIID. [19]. The disease is caused by mutations of four genes encoding these enzymes: lysosomal aN-acetylglucosaminidase (type IIIA MPS) - the gene is mapped to 17q25.3, acetyl-CoA-α-glucosaminide-N-acetyltransferase (type IIIB MPS - the gene is mapped to 17q21.2, lysosomal N-acetylglucosamine-6-sulfatase (MPS IIIC type - the gene is mapped to 8 p11.2-p11.1, sulfamidase (MPS IIID type) - the gene is mapped to 12q14.3. All enzymes are involved in the metabolism of heparan sulfate, the accumulation of which causes severe CNS disorders More than 200 mutations have been registered in these genes that lead to the development of various types of MPS III, and their number continues to grow [25].

The main clinical manifestations of type III MPS are progressive disorders of the central nervous system, dementia syndrome, severe behavioral disorders, chronic diarrhea. Symptoms include sensorineural deafness, joint contracture, and moderate facial roughness. In children, shortness of breath often occurs at an early age, but the symptoms gradually subside. This often occurs in the 2nd year of life. Patients with MPS III are more likely to have hepatomegaly than splenomegaly [7,19,25].

**Mucopolysaccharidosis type IV.** Mucopolysaccharidosis type IV (Morquio syndrome) was described in 1929 by pediatrician Morkio L. and British doctor Brailsford J.F. This disease is associated with a defect in N-acetylgalactosamine-6-sulphate sulfatase (MPS type IVA)-16q24.3 due to a mutation in the GALNS gene and a defect in β-galactosidase (MPS type IVB)-3p22.3 due to a mutation in the GLB1 gene . These enzymes are involved in the metabolism of keratan sulfate and chondroitin sulfate.

The incidence ranges from 76,000 to 1 in Northern Ireland and from 64 to 1 million newborns in Australia [11].

The genetic type is autosomal recessive inheritance. More than 220 mutations leading to the development of the disease have been registered in the GALNS gene [14].

The main clinical manifestations are short stature, keeled chest, skeletal deformity, increased mobility of small joints, etc. It is important to note that children with Morquio syndrome have normal intelligence [31, 100, 107, 160, 256]. Patients have visual and hearing impairments, hepatomegaly, and lesions of the respiratory and circulatory systems [11,22].

Type IV MPS disease has a progressive type of course. The onset age is 1–3.5 years, although the final diagnosis is delayed for many years (3–15 years) and is characterized by progressive valgus deformity of the knee joints, kyphosis, growth retardation against the background of a disproportionate shortening of the trunk and neck, and “duck gait” . The clinical picture is dominated by skeletal deformities in the form of spondyloepiphyseal dysplasia with secondary neurological complications. The main features of Morquio syndrome, which are not found in other types of MPS, are small joint hypermobility and wrist deformity. Hip subluxation and knee instability are common in patients with type IV MPS. The combination of dentate hypoplasia and ligamentous laxity can lead to instability of the atlas axis, which can subsequently lead to narrowing of the spinal canal and compression of the spinal cord [3,4].

Most patients have a classic disease phenotype, but some patients may have serious impairments in other systems, such as cardiopulmonary failure, even if they do not have typical outward symptoms [5].

The life expectancy of patients with type IV MPS can vary from 10 to 20 years, but there is also a certain percentage of patients who survive to an older age. In patients with Morquio syndrome, respiratory dysfunction is one of the main concerns. This may be caused by obstructive or restrictive processes. Destructive diseases can develop due to shortening or deformity of the chest and impaired mobility of the diaphragm. Obstructive sleep apnea syndrome (OSAS)

**Table1**

**Pathology of the cardiovascular system**

| Sign | MPS I | MPS II | MPS III | MPS IV | MPS VI | MPS VII | MPS IX | MPS-PS |
|---|---|---|---|---|---|---|---|---|
| Age of manifestation of CCC pathology | 6-24 months. | 3-8 years; benign form 10-15 years | 2-6 years | 1-3.5 years | The first year of life | The first year of life | The first year of life | 4 months |
| Pathology of the valve apparatus | + | + | + | + | + | + | | + |
| Pathology of the mitral valve | + | + | + | + | + | | | + |
| Pathology of the aortic valve | + | + | + | + | + | | | + |
| Pathology of the tricuspid valve | + | + | + | + | + | | | + |
| Pathology of the pulmonary valve | + | + | | | + | | | + |
| Cardiomyopathy | + | + | + | + | + | + | | + |

Table2

**Respiratory system injury**

| Type of MPC | Chronic bronchitis | Apnea | Pneumonia | Noisy breathing |
|---|---|---|---|---|
| MPS I | + | + | + | + |
| MPS II | + | + | + | + |
| MPS III | + | + | + | + |
| MPS IV | | + | | + |
| MPS VI | + | + | + | + |
| MPS VII | + | + | | |
| MPS IX | | | | |
| MPS-ПС | + | + | + | + |

is one of the first signs of damage to the respiratory system. An abnormally high heart rate and arterial hypertension have been reported in adult patients. Respiratory disturbances characteristic of this type of MPS can lead to cardiovascular complications, such as pulmonary hypertension with subsequent development of cor pulmonale [3,4,5,11,22].

**Mucopolisaccharidosis type VI.** Patients with type VI MPS (Maroteau-Lami syndrome) were first reported in 1963 by Dr. Pierre Maroteau and Dr. Maurice Lamy (84). The incidence rate was 320,000 per birth [20].

The prevalence of type VI MPS in patients with different types of MPS ranges from 2% to 4% [88,89] in Scandinavia (Sweden, Norway, Denmark) to 8% (301) in the Netherlands. Selective screening in Brazil and northern Portugal has shown a higher risk of having children with Marotto-Lami syndrome. Patients with MPS VI in these countries were diagnosed in 18.5%, and in patients with various types of MPS, 16% were diagnosed [31].

The genetic form is autosomal recessive inheritance. This disease is caused by mutations in the ARSB gene. The gene is mapped on the long arm of chromosome 5 (5q13-5q14). It is known that there are more than 130 mutations in the ARSB gene, leading to the development of the disease. The absence or decrease in the activity of arylsulfatase B (N-acetylgalactosamine-4-sulfatase) leads to the deposition of dermatan sulfate in lysosomes. Chondroitin 4-sulfate is also a pathogenetic factor in the development of the disease [1].

Arylsulfatase B is an important enzyme involved in the structure of connective tissue. With a deficiency, lesions of the musculoskeletal system, cardiovascular system, and respiratory system develop. Studies by a group of scientists have shown that the accumulation of dermatan sulfate contributes to the development of pathological changes in the cardiovascular system and damage to the joints [4].

The clinical manifestations of the disease are heterogeneous, and their onset ranges from a few months to 10 years. The first symptoms are usually detected in the 1st year of life, but there are also cases when the disease progresses slowly [3]. In rapidly progressive Maroteau-Lami syndrome, patients experience significant growth retardation, and by 3–4 years of age, growth stops, reaching 120 cm [20]. Stiffness of large and small joints, respiratory failure, heart failure, etc. will gradually increase. Early rough facial features of the gargoylism type are observed, such as protruding frontal tubercles, sunken bridge of the nose, macroglossia, gingival hypertrophy, delayed teething. Hirsutism, chest deformity, contracture, scoliosis and kyphosis, hepatosplenomegaly, umbilical and inguinal hernia, noisy breathing, shortness of breath, rhinitis, sinusitis, and otitis media are common in most patients. In addition to progressive corneal opacity, damage to the optic nerves due to compression and hydrocephalus can also lead to visual impairment [5]. In the second year of life, he develops severe obstructive pulmonary disease and respiratory failure requiring tracheostomy. It should be noted that the intellectual development of the patient remains within the normal range. Stenosis or regurgitation of the heart valve requires arthroplasty, and complications requiring surgical intervention appear with age. Severe damage to the joints, especially the hip, requires arthroplasty. Median nerve decompression is necessary for toe deformity due to carpal tunnel syndrome. With severe spinal deformity, stenosis of the spinal canal in the cervical region also requires surgical correction [20].

The slowly progressive form of Maroteau-Lami syndrome is characterized by a slow onset of clinical symptoms. However, even if it progresses slowly after the second decade, orthopedic complications, valvular heart disease, and deterioration in lung function may develop [31].

Recently, intermediate types have begun to be described, since there are no clear descriptive criteria for determining the severity. For example, severe symptoms can develop within a single system to the point of requiring major surgical intervention [3].

**Mucopolysaccharidosis type VII.** Sly's syndrome is a rare disease among mucopolysaccharidoses. The defective GUSB gene responsible for the development of the clinical picture of Sly's syndrome is located on the long arm of the 7th chromosome (7q21.1-11). Not a single case has been registered in Russia, it occurs in less than 1 in 1,250,000 newborns. In fact, this disease develops in the womb, and most babies who develop it die before or shortly after birth. If it is not severe, then in the 1st year of life the same signs appear as in the Hurler syndrome.

Type of inheritance - autosomal recessive. The essence of the disease lies in the deficiency of an enzyme called β-glucuronidase, which decomposes mucopolysaccharides (glycosaminoglycans, GAGs). GAG degradation products accumulate in the tissues of many organs, leading to the development of pathology. In Sly's syndrome, edema and hyperplasia of many organs usually appear earlier and are more pronounced than in other types of mucopolysaccharidosis. First, hydrocephalus (cerebral edema), enlarged liver and spleen are detected.

Anomalies in the development of a fetus with Sly's syndrome can be detected with regular ultrasound examinations in the 2nd or 3rd trimester; in this case, prenatal diagnosis is additionally performed with amniocentesis and measurement of enzyme activity. However, because it is an extremely rare disease, the significance of the β-glucuronidase enzyme is rarely tested. The most severe cases of MPS VII are characterized by high water pregnancies or excessive accumulation of fluid in the tissues of the fetus, which can lead to the death of the baby before or shortly after birth. The symptoms and stages are varied due to the variety of mutations in the genes themselves. In mild cases of Sly syndrome, neonatal jaundice may occur. The mild form of MPS VII, like many other mucopolysaccharides, develops at the age of 1 year. These include coarse facial features and

a flat bridge of the nose, a large disproportionate head (megacephaly), umbilical and inguinal hernias, a very large abdomen due to abnormal enlargement of the liver and spleen, and delayed physical development (inability to roll from the abdomen to the back or maintain a sitting position). After 1 year, hypoplasia and multiple bone malformations become noticeable. Between the ages of 7 months and about 8 years, clouding of the cornea of the eye may occur. As the disease progresses, hearing loss, speech delay (not necessarily with intellectual impairment), recurrent upper respiratory tract infections, heart disease, and hirsutism (excessive growth of facial and body hair appear) [2, 13, 18, 23, 31].

**Mucopolysaccharidosis type IX.** Mucopolysaccharidosis type IX is caused by a deficiency in an enzyme called hyaluronidase 1 (Hyal-1), which breaks down hyaluronic acid (HA). MPS type IX is the rarest MPS, with only 4 patients reported to date. In 1996, the first MPS IX patients with periarticular soft tissue masses and nodular hyperplasia, short stature, and acetabular erosion were reported [46]. In 2011, Imundo and colleagues reported that 3 brothers from the Middle East developed juvenile idiopathic arthritis (JIA) [Imundo et al. 2011]. All reported patients with MPS IX had joint and bone problems. Other symptoms included short stature, cysts, frequent ear infections, and lupus (suppositories) [17].

**Mucopolysaccharidosis-plus syndrome.** MPS-PS is a new hereditary disease, identified and described in 2017 by a group of scientists from Yakutia and Japan, Turkey [Kondo et al., 2017; Dursun et al., 2017] molecular genetic cause of autosomal recessive disease mutation in the VPS33A gene (NM_022916.4: c.1492C> T, NP_075067.2: p.Arg498Trp), VPS33A gene (NM_022916.4: c.1492C> T, NP_075067.2: p.Arg498Trp, hereinafter referred to as p.R498W). The VPS33A gene is mapped and located on chromosome 12q24.31 and contains 13 exons. The mutation is located in exon 12, which codes for domain 2 of the VPS33A protein. To date, only p.R498W has been described as a mutation that leads to the development of this disease and the accumulation of heparan sulfate in the urine and plasma of patients. MPS-PS leads to multisystem damage to organs and systems with signs of lysosomal mucopolysaccharidosis accumulation disease. The frequency of the mutant allele among the Yakut population is 1:81 and 0: 1218 among the Turkish population. The predicted value of the incidence rate in the Republic of Sakha (Yakutia) is 1: 12000 newborns. The new disease was entered into the McCusick international database under the number OMIM # 617303 and was named mucopolysaccharidosis-plus syndrome (MPS-PS).

The clinical course of patients is similar to that of other types of MPS. A characteristic feature of MPS-PS is early manifestation of the disease and early infant mortality, multisystem organ damage - lungs, kidneys (secondary nephrotic syndrome, severe proteinuria 2–3 g / day, nephromegaly, the activity of enzymes involved in GAG metabolism was within normal limits) , heart (septal heart disease and severe course), central nervous system and damage to the hemopoietic system (severe anemia requiring blood transfusion, coagulopathy with hemorrhagic syndrome) [22,31].

**Conclusion.** Since mucopolysaccharide disease was first reported in 1917, thousands of cases have been reported worldwide. MPS are multisystemic diseases, most of them are characterized by phenotypic features, which makes it possible to suspect the diagnosis “at first sight” of a person of the type of “gargoylism”. A rather striking feature of MPS is multiple dysostosis. Of course, the idea of MPS is formed on the basis of a comparison of clinical and instrumental data, and the final diagnosis can only be verified using laboratory methods. Knowledge of the onset and characteristics of the various subtypes of MPS allows for early diagnosis, which is essential for maintaining organic function and improving quality of life.

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# ISOLATED SPINAL CORD INJURY IN CHILDREN - SCIWORA SYNDROME

The relevance of the isolated injury of the spinal cord in children is due to the severity of damage, which often leads to unsatisfactory results of the therapy. Objective. Analyse and legend in the form of an overview of literature Scientific products. Materials and methods. Scientific publications to write a review of literature were obtained from the PabMed, eLIBRARY, CYBERLENINKA. Literature sources were searched for the following keywords: isolated spinal cord injury, SCIWORA syndrome, SCIWONA syndrome, SCIWORET syndrome. Results and discussion. SCIWORA syndrome diagnostic frequency among children who have been injured by the postcase is from 3% to 6% of cases. Initially, this syndrome is to meet fishing up to 8 years of age, boys predominate among the victims. Most often other parts of the spinal cord are affected cervical. Lead to the development of SCIWORA syndrome car accident. The main clinical symptoms of diseases are weakness in the limbs, the feeling of the passage of the "electric current" on the spine, various neurological disorders: from a minor deficit to the complete absence of motor and sensitive functions. The severity of neurological coupling will determine the scale of F. Frankel and the ASIA scale. The leading diagnostic method is the magnetic-reserved tomography. The patient's treatment with SCIWORA syndrome conducts conservative and operational methods, while the standard of therapy is currently not developed. The most important projection criteria during SCIWORA syndrome is the initial neurological status of patients after injury and results magnetic resonance tomography. Children with the lightest in neurologically delicacy are restored completely. Conclusion. SCIWORA syndrome problem keeping your apartment. The necessary developed uniform approaches and standards in the tactics of the treatment of children with this melting pathology.

**Keywords:** children, isolated spinal cord injury, SCIWORA syndrome, literature review.

**Introduction.** The isolated injury of the spinal cord in children is an actual problem of modern traumatology and neurosurgery [26, 31, 32]. The relevance is due to the severity of damage gained by children, which often leads to unsatisfactory results of the therapy [22, 37]. In the domestic medical literature devoted to the spinal-spinal injury in children, aspects of SCIWORA syndrome - isolated spinal cord injury without related damage to the bone structures of vertebrals and intervertebral discs are not fully reflected.

**Objective.** Analyze the main domestic and foreign publications dedicated to isolated spinal cord injuries in children - SCIWORA syndrome. The obtained information is recycled and submit in the form of a review of literature.

**Material and methods.** Scientific publications To write a review of literature on the topic "Isolated spinal cord injury in children - SCIWORA syndrome" were obtained from modern PubMed, eLIBRARY, CYBERLENINNKA databases. A total of 42 scientific articles were used, which reflect the most actual problems and aspects of the topic studied. Domestic literary sources used - 4 (9.53%), foreign - 38 (90.47%).

The search for literature sources was carried out according to the following keywords: isolated spinal cord injury in children, SCIWORA syndrome, SCIWONA syndrome, SCIWORET syndrome.

**Results and discussion.** One of the first authors who reported the damage to the spinal cord in children without X-ray confirmations from the vertebrae and the spine binder, was S. Lloyd, published on this topic in 1971 [16]. The decade later, at the beginning of the 80s of the last century, the american authors of D. Peng et al., presented the medical community to the publication, in which 20-year-old clinical experience was set forth on a scientific basis about 24 children without radiation (x-ray and computer-tomographic (CT)) symptoms characteristic of the injuries of the vertebrae. This state of the authors have been defined as «Spinal Cord Injury Without Radiographic Abnormality» (abbreviated: SCIWORA) [21].

With a wide introduction into the clinical practice of magnetic resonance tomography (MRI), when it became possible to diagnose even minor damage to the spinal cord, a new term was proposed – SCIWONA (Spinal Cord Injury Worth Neuroimaging Abnormality). This abbreviation describes the clinical situations of damage to the spinal cord in children and adolescents unchanged on the MRI grams of the spine and the spinal cord [42]. In cases where the damage to the spinal cord is diagnosed in the absence of reliable history data on injuries, the term SCIWORET is used (Spinal Cord Injury Worth Radiographic Evidence of Trauma) [10].

In English-speaking medical literature, when describing the isolated spinal cord injuries in children, the term "SCIWORA" was the greatest distribution. Pathological conditions, regarded as "SSIWONA" and "SCIWORET" in pediatric patients describe significantly less often [41]. Scientific publications in foreign literature dedicated to SCIWORA syndrome sufficiently, which cannot be said about articles in domestic sources [4]. Even in the regulatory medical activities of documents, in relation to the spinal-spinal inju-

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